REMARKS

I. Status of the claims

Claims 1-22 are pending. No claim has been amended.

Claims 1-19, 21, and 22 are allowed. Claim 20 is the sole rejected claim.

II. Rejection under 35 U.S.C. § 112, first paragraph

Claim 20 is rejected under 35 U.S.C. § 112, first paragraph. Office Action, pp. 2-3. The Examiner asserts that "the specification, while being enabled for reducing the activity of a neurotensin receptor, does not reasonably provide enablement for the treatment of schizophrenia, Parkinson's disease, and Alzheimer's disease." *Id.* Applicants respectfully traverse this rejection.

Applicants respectfully submit that the Examiner has not met her burden to establish a *prima facie* case for lack of enablement. A disclosure for making and using that corresponds to the scope of the claimed subjected is presumed compliant with the enablement requirement. M.P.E.P. § 2164.04; *In re Marzocchi*, 439 F.2d 220 (C.C.P.A. 1971). The burden is on the Examiner to establish a reasonable basis to question the enablement of the claimed invention. *Id.*; *In re Wright*, 999 F.2d 1557, 1562 (Fed. Cir. 1993). To determine enablement, the Examiner is required to assess whether one skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988); *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993); M.P.E.P. § 2164.01. The eight Wands factors (sometimes called the Forman factors) are used to assess undue experimentation, and are delineated in

M.P.E.P. § 2164.01(a). *In re Wands*, 858 F.2d 731 *citing In re Forman*, 230 USPQ 546, 547 (Bd. Pat. App & Int 1986); M.P.E.P. § 2164.01(a). To conclude a lack of enablement resulting from undue experimentation, the Examiner must not rely on a single factual determination, but must weigh many factual considerations including the Wands factors. *In re Wands*, 858 F.2d at 737; M.P.E.P. § 2164.01(a). The courts have held that a "considerable amount of experimentation is permissible . . . if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *In re Wands*, 858 F.2d at 737 *citing In re Jackson*, 217 U.S.P.Q. 804, 807 (Bd. App. 1982); See M.P.E.P. § 2164.06.

Also, a "rigorous correlation [between *in vitro* utility and *in vivo* activity] is not necessary where the disclosure of pharmacological activity is reasonably based upon probative evidence." Cross v. Iizuka, 753 F.2d 1040, 1050 (Fed. Cir. 1985); M.P.E.P. § 2164.02. Here, because probative evidence has been provided by example 4 on pages 34-35 of the specification and the passages cited below, this claim is fully enabled for all three diseases.

Further, Applicants respectfully submit that the Examiner has simply asserted that enablement is lacking, but has discussed, at most, only one of the Wands factors. Thus, as discussed in detail below, the Examiner's rejection has not met the burden set forth by the courts and as instructed by the M.P.E.P. to establish a prima facie case for a lack of enablement.

Alzheimer's disease

The Examiner alleges that none the of art submitted shows that neurotensin receptor-affecting compounds that inhibit the neurotensin receptor proteins expressed from HEK membranes can be used to treat Alzheimer's disease. First, the burden is on the Examiner to show lack of enablement because, as discussed above, enablement is presumed compliant. The Examiner does not discuss any factual considerations (at best ,only an opinion is expressed), let alone the multiple considerations, including the Wand factors, required to establish a prima facie case of nonenablement. Thus, the Examiner has not met her burden to refute the presumed enablement. Second, the Examiner has not provided evidence that the source of neurotensin receptor protein influences the ability to predict treatability of Alzheimer's disease with neurotensin receptor-affecting compounds. If the Examiner wishes to make this claim, then she must provide evidence that such a difference exists to rebut the presumed enablement; the extant conclusory statement, in the absence of evidence, is insufficient to do so.

Furthermore, although Applicants do not admit that the Examiner has made a prima facie case for a lack of enablement, Applicants provide evidence that the claim is indeed enabled for Alzheimer's disease. Support for treating Alzheimer's disease can be found in U.S. Pat. No. 5,840,682 to Clerc et al. at, for example, col. 5 line 61 to col. 6 line 40, col. 20 line 66 to col. 21 line 15, and claim 19; U.S. Pat. No. 5,204,354 to Chakravarty et al. at, for example, col. 2 lines 1-5; U.S. Pat. No. 5,747,303 to Debernard et al. at, for example, col. 6 line 41 to col. 7 line 20; and WO 94/10151 at, for example, page 3 lines 17-25, and page 26 to page 28 line 20. Taken together these statements

indicate that persons skilled in the art believe that neurotensin receptor-affecting compounds can be used to treat Alzheimer's disease; the Examiner has pointed to no evidence to refute the statements in these references. For at least the reasons stated above, Applicants respectfully submit that claim 20 is enabled, at least, for the treatment of Alzheimer's disease.

Parkinson's disease

The Examiner argues that Antonelli "fails to show that selective antagonists alone are effective in treating Parkinson's disease." Office Action, p. 2. First, the burden is on the Examiner to show lack of enablement because, as discussed above, enablement is presumed compliant. The Examiner, at best, discusses a single factual consideration, but not the multiple considerations, including the Wand factors, required to establish a prima facie case of nonenablement. Thus, the Examiner has not met her burden to refute the presumed enablement. Second, just because another compound is used with the Antonelli treatment, does not refute the presumed enablement because Applicant's claimed method recites an method for treating comprising at least one compound of claim 1. Thus, the claim does not exclude administering other compounds in the treatment. Third, the data and cited passages from Chinaglia (see below) show that neurotensin receptor-affecting compounds affect neurotensin receptor binding and therefore would be useful for treating Parkinson's disease. Thus, this is additional evidence for the enablement of treating Parkinson's disease with a neurotensin receptor affecting compound.

Furthermore, although Applicants do not admit that the Examiner has made a prima facie case for a lack of enablement, Applicants provide evidence that the claim is indeed enabled for Parkinson's disease. Support for treating Parkinson's disease can be found in U.S. Pat. No. 5,840,682 to Clerc et al. at, for example, col. 5 line 61 to col. 6 line 40, col. 20 line 66 to col. 21 line 15, and claim 16; Chinaglia et al. (Neuroscience, Vol. 39, No. 2, pp. 351-360 (1990)) at, for example, the paragraph bridging pages 351 and 352, the first full paragraph of page 352, and col. 2 of page 358; U.S. Patent No. 5,430,047 to Johnson et al. at, for example, Abstract, col. 1 lines 22-51, col. 7 lines 46-64, col. 15 lines 3-20, and claim 6; U.S. Pat. No. 5,204,354 to Chakravarty et al. at, for example, col. 3 lines 17-20; U.S. Pat. No. 5,747,303 to Debernard et al. at, for example, col. 6 line 41 to col. 7 line 20; and WO 94/10151 at, for example, page 3 lines 17-25, and page 26 to page 28 line 20. Taken together these statements indicate that persons skilled in the art believe that neurotensin receptor-affecting compounds can be used to treat Parkinson's disease; the Examiner has pointed to no evidence to refute the statements in these references. For at least the reason stated above, Applicants respectfully submit that claim 20 is enabled, at least, for the treatment of Parkinson's disease.

Schizophrenia

The Examiner alleges that Binder et al. suggests that not all schizophrenic patients would be helped by being treated with neurotensin receptor affecting compound. First, the burden is on the Examiner to show lack of enablement because,

as discussed above, enablement is presumed compliant. The Examiner, at best, discusses a single factual consideration, but not the multiple considerations, including the Wand factors, required to establish a prima facie case of nonenablement. Thus, the Examiner has not met her burden to refute the presumed enablement. Second, even if some schizophrenic patients are not helped by being treated with neurotensin receptor affecting compound (which Applicants do not admit), the claim is still fully enabled. There is no requirement that ALL patients must be treatable because such a requirement would be unreasonable; there are no antibiotics that can treat all bacterial infections (and thus cannot treat all patients) and yet a claim to treat bacterial infections using, for example, Erythromycin would surely be enabled. Further, even if the claim was not fully enabled due to not all schizophrenic patients being helped with the claimed treatment (which the Applicants do not admit), the claim is still enabled because the presence of inoperable subject matter within the scope of a claim does not, by itself, render the claim nonenabled. *Atlas Powder Co. v. E. I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1577 (Fed. Cir. 1984); M.P.E.P. § 2164.08(b). Moreover, enablement of a genus only requires enablement of representative species within that genus. M.P.E.P. § 2164.02. Third, the Examiner's quote from Binder et al. is taken out of context. In reading the entire reference (indeed even the rest of the abstract) there is considerable evidence that neurotensin receptor affecting compounds can be used to treat schizophrenia. Specifically, Applicants point to the entire abstract, the bridging paragraph of pages 857-58, and the first full paragraph of col. 2 on page 866. These passages, as well as the article when read as a whole, show that neurotensin receptor affecting compounds can be used to treat schizophrenia.

Furthermore, although Applicants do not admit that the Examiner has made a prima facie case for a lack of enablement, Applicants provide evidence that the claim is indeed enabled for schizophrenia. Support for treating schizophrenia can be found in U.S. Pat. No. 5,840,682 to Clerc et al. at, for example, col. 5 line 61 to col. 6 line 40, col. 20 line 66 to col. 21 line 15, and claim 16; U.S. Patent No. 5,430,047 to Johnson et al. at, for example, Abstract, col. 1 lines 22-51, col. 7 lines 46-64, col. 15 lines 3-20, and claims 5 and 6; U.S. Pat. No. 5,204,354 to Chakravarty et al. at, for example, col. 3 lines 11-19; U.S. Pat. No. 5,747,303 to Debernard et al. at, for example, col. 6 line 41 to col. 7 line 20; Binder et al. (Biol Psychiatry, vol. 50 pp. 856-872 (2001)) at, for example, entire Abstract, paragraph bridging p. 857 and p. 858, first full paragraph p. 866 col. 2; and Berod et al. (Current Opinion in Pharmacology, vol. 2, pp. 93-98 (2002)) at, for example, second paragraph of Conclusions on p. 96. Taken together these statements indicate that persons skilled in the art believe that neurotensin receptor-affecting compounds can be used to treat schizophrenia; the Examiner has pointed to no evidence to refute the statements in these references. For at least the reason stated above, Applicants respectfully submit that claim 20 is enabled, at least, for the treatment of schizophrenia.

Overall, for at least the aforementioned reasons, withdrawal of this rejection is earnestly solicited.

III. Conclusion

In view of the foregoing remarks, Applicants respectfully request the reconsideration and reexamination of this application and the timely allowance of all pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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Enclosures:

U.S. Pat. No. 5,840,682
U.S. Pat No. 5,430,047
U.S. Pat No. 5,204,354
U.S. Pat. No. 5,747,303
WO 94/10151
T. Antonelli, et al., Journal of Neuroscience Research, Vol. 70, pp. 766-773 (2002).
E. B. Binder, et al., Biological Psychiatry, Vol. 50, pp. 856-872 (2001).
A. Bérod et al., Current Opinion in Pharmacology, Vol. 2, pp. 93-98 (2002).
Chinaglia et al. Neuroscience, Vol. 39, No. 2, pp. 351-360 (1990).